

WHAT IS CLAIMED IS:

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1. A sustained release nail varnish composition comprising:
 - (a) a pharmaceutically effective agent;
 - (b) a humectant;
 - (c) water;
 - (d) less than about 7.5% (w/w) based on the total weight of the composition, of a polymeric film-forming agent;
 - (e) at least one additional excipient; and
 - (f) a solvent system including at least one volatile solvent.

2. The nail varnish of claim 1, wherein said pharmaceutically effective agent is selected from the group consisting of an antifungal agent, a keratolytic agent and mixtures thereof.

3. The nail varnish of claim 2, wherein said antifungal agent is selected from the group consisting of amphotericin B, butefanine, butoconazole, carbol-fuchsin, ciclopirox, clioquinol, clotrimazole, econazole, gentian violet, ketoconazole, miconazole, naftifine, nystatin, oxiconazole, sodium thiosulfate, terbinafine, terconazole, tolnaftate, undecylenic acid,

therapeutically acceptable salts thereof, derivatives thereof and mixtures thereof.

4. The nail varnish of claim 3, wherein said antifungal agent is clotrimazole or miconazole nitrate.

Sub 12 } 5. The nail varnish of claim 2, wherein said antifungal agent is present in an amount of less than about 1% (w/w), relative to the total weight of the composition.

6. The nail varnish of claim 2, wherein said antifungal agent is present in an amount of less than about 5% (w/w) based on the weight of the non-volatile components.

Sub B3 } 7. The nail varnish of claim 2, wherein said keratolytic agent is selected from the group consisting of urea, sulfur, salicylic acid, podophyllum resin and mixtures thereof

8. The nail varnish of claim 2, wherein said keratolytic agent is

~~urea.~~

Sub A3 } 9. The nail varnish of claim 2, wherein said keratolytic agent is present in an amount of less than about 1% (w/w) relative to the total weight of the composition.

10. The nail varnish of claim 2, wherein said keratolytic agent is present in an amount of from about 0.05% to about 5% (w/w) based on the weight of the non-volatile components.

Sub B3 } 11. A nail varnish of claim 2, wherein said pharmaceutically effective agent further comprises an antibacterial agent, an antiviral agent, an antipsoriatic agent or mixtures thereof.

12. A nail varnish of claim 11, wherein said antibacterial agent is selected from the group consisting of bacitracin, clindamycin, erythromycin, gentamicin, mupirocin, neomycin, tetracyclines, polymyxin B, benzalkonium chloride, boric acid, hexachlorophene, iodine, iodoquinol, mafenide, mercury ammoniated, metronidazole, nitrofurazone, selenium sulfide, silver

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13. The nail varnish of claim 11, wherein said antibacterial agent is present in an amount of from about 0.01% to about 1% (w/w), relative to the total weight of the composition.

14. The nail varnish of claim 11, wherein said antibacterial agent is present in an amount of from about 0.05% to about 5% (w/w), based on the weight of the non-volatile components.

15. A nail varnish of claim 11, wherein said antiviral agent is selected from the group consisting of acyclovir, amantadine, cidofovir, famciclovir, foscarnet, ganciclovir, paliuizumab, penciclovir, ribavirin, rimantadine, valcyclovir, salts thereof, derivatives thereof, and mixtures thereof.

16. The nail varnish of claim 11, wherein said antiviral agent is present in an amount of from about 0.08% to about 0.8% (w/w), relative to the total weight of the composition.

17. The nail varnish of claim 11, wherein said antiviral agent is present in an amount of from about 0.8% to about 8% (w/w), based on the weight of the non-volatile components.

18. A nail varnish of claim 11, wherein said antipsoriatic agent is selected from the group consisting of alclometasone, amcinonide, betamethasone, clobetasol, clocortolone, desonide, desoximetasone, diflorasone, fluocinolone, ~~fluocinonide~~, flurandrenolide, halcinonide, hydrocortisone, mometasone, prednicarbate and triamcinolone, salts thereof, derivatives thereof, and mixtures thereof.

19. The nail varnish of claim 11, wherein said antipsoriatic agent is present in an amount of from about 0.02% to about 2% (w/w), relative to the total weight of the composition.

20. The nail varnish of claim 11, wherein said antipsoriatic agent is present in an amount of from about 0.1% to about 10% (w/w), based on the weight of the non-volatile components.

21. The nail varnish of claim 1, wherein said humectant is selected from the group consisting of glycerol, sorbitol and mixtures thereof.

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A7 → 22. The nail varnish of claim 1, wherein said humectant is present in an amount of from about 3% to about 15% (w/w), relative to the total weight of the composition.

23. The nail varnish of claim 1, wherein said humectant is present in an amount of from about 5% to about 35% (w/w), based on the weight of the non-volatile components.

24. The nail varnish of claim 1, wherein said water is present in an amount of less than about 5% (w/w), relative to the total weight of the composition.

25. The nail varnish of claim 1, wherein said water is present in an amount of from about 0.4% to about 25% (w/w), based on the weight of the non-volatile components.

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26. The nail varnish of claim 1, wherein said polymeric film-forming agent is selected from the group consisting of hydrophobic (water insoluble) polymers.

27. The nail varnish of claim 26, wherein said hydrophobic (water insoluble) polymer is selected from the group consisting of hydrophobic cellulose derivatives, hydrophobic methacrylic polymers, cellulose acetate phthalate, shellac, (derivatives thereof), and mixtures thereof. *remove parentheses*

28. The nail varnish of claim 27, wherein said hydrophobic cellulose derivative is selected from the group consisting of ethyl cellulose of any acceptable molecular weight. *112*

29. The nail varnish of claim 27, wherein said hydrophobic methacrylic polymer is selected from the group consisting of methacrylic acid copolymer type B (USP/NF), methacrylic acid copolymer type C (USP/NF), ammonio methacrylate copolymer type B (USP/NF) and ammonio methacrylate copolymer type A (USP/NF), derivatives thereof, and mixtures

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thereof.

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AG → 30. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in an amount of from about 8% to about 35% (w/w), based on the weight of the non-volatile components.

31. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antifungal agent from about 1:0.01 to about 1:0.3.

32. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to keratolytic agent from about 1:0.01 to about 1:1.

33. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antibacterial agent from about 1:0.01 to about 1:0.3.

34. The nail varnish of claim 1, wherein said polymeric film-forming

agent is present in a weight ratio of polymer to antiviral agent from about 1:0.02 to about 1:0.2.

35. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antipsoriatic agent from about 1:0.006 to about 1:0.15.

36. The nail varnish of claim 1, wherein said at least one additional excipient is selected from the group consisting of plasticizers.

37. The nail varnish of claim 36, wherein said plasticizer is selected from the group consisting of dibutyl sebacate, diethyl phthalate, lanolin alcohols, mineral oil, petrolatum, polyethylene glycol, propylene glycol, triacetin, triethyl citrate, and mixtures thereof.

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A9 } 38. The nail varnish of claim 36, wherein said plasticizer is present in an amount of from about 0.1% to about 2% (w/w), relative to the total weight of the composition.

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39. The nail varnish of claim 36, wherein said plasticizer is present in an amount of from about 0.5% to about 10% (w/w), based on the weight of the non-volatile components.

40. The nail varnish of claim 36, wherein said plasticizer is present in a weight ratio of plasticizer to polymer from about 0.04:1 to about 0.3:1.

41. The nail varnish of claim 1, wherein said volatile solvent is selected from the group consisting of an alcohol, a ketone, and mixtures thereof.

42. The nail varnish of claim 41, wherein said alcohol is selected from the group consisting of ethanol, isopropyl alcohol, methanol and mixtures thereof, and further wherein said ketone is acetone.

43. The nail varnish of claim 1, wherein said volatile solvent is a mixture of acetone and isopropyl alcohol.

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44. The nail varnish of claim 1, wherein said volatile solvent is

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present in an amount of from about 60% to about 90% (w/w), relative to the total weight of the composition.

45. The nail varnish of claim 43, wherein said acetone and said isopropyl alcohol are present in a volumetric ratio of acetone to isopropyl alcohol from about 1:4 to about 4:1.

46. The nail varnish of claim 1, wherein said solvent system further includes at least one non-volatile solvent selected from the group consisting of benzyl alcohol, benzyl benzoate, corn oil, cottonseed oil, ethyl oleate, glycerin, glycofural, isopropyl myristate, isopropyl palmitate, mineral oil, peanut oil, polyethylene glycol, propylene glycol, propylene carbonate, sesame oil, soybean oil, water, and mixtures thereof.

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47. A sustained release nail varnish composition comprising:

- (a) an antifungal agent;
- (b) a keratolytic agent;
- (c) a humectant;
- (d) water;

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- (e) a polymeric film-forming agent;
- (f) at least one additional excipient; and
- (g) a solvent system including at least one volatile solvent.

48. The nail varnish of claim 47, wherein said antifungal agent is selected from the group consisting of amphotericin B, butefanine, butoconazole, carbol-fuchsin, ciclopirox, clioquinol, clotrimazole, econazole, gentian violet, ketoconazole, miconazole, naftifine, nystatin, oxiconazole, sodium thiosulfate, terbinafine, terconazole, tolnaftate, undecylenic acid, therapeutically acceptable salts thereof, derivatives thereof and mixtures thereof.

49. The nail varnish of claim 48, wherein said antifungal agent is clotrimazole or miconazole nitrate.

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50. The nail varnish of claim 47, wherein said antifungal agent is present in an amount of less than about 1% (w/w), relative to the total weight of the composition.

51. The nail varnish of claim 47, wherein said antifungal agent is present in an amount of less than about 5% (w/w) based on the weight of the non-volatile components.

52. The nail varnish of claim 47 , wherein said keratolytic agent is selected from the group consisting of urea, sulfur, salicylic acid, podophyllum resin and mixtures thereof

53. The nail varnish of claim 47, wherein said keratolytic agent is urea.

54. The nail varnish of claim 47, wherein said keratolytic agent is present in an amount of less than about 1% (w/w) relative to the total weight of the composition.

55. The nail varnish of claim 47, wherein said keratolytic agent is present in an amount of from about 0.05% to about 5% (w/w) based on the weight of the non-volatile components.

56. The nail varnish of claim 47, further comprising an antibacterial agent, an antiviral agent, an antipsoriatic agent or mixtures thereof.

57. The nail varnish of claim 56, wherein said antibacterial agent is selected from the group consisting of bacitracin, clindamycin, erythromycin, gentamicin, mupirocin, neomycin, tetracyclines, polymyxin B, benzalkonium chloride, boric acid, hexachlorophene, iodine, iodoquinol, mafenide, mercury ammoniated, metronidazole, nitrofurazone, selenium sulfide, silver sulfadiazine, salts thereof, derivatives thereof and mixtures thereof.

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A14 7 58. The nail varnish of claim 56, wherein said antibacterial agent is present in an amount of from about 0.01% to about 1% (w/w), relative to the total weight of the composition.

59. The nail varnish of claim 56, wherein said antibacterial agent is present in an amount of from about 0.05% to about 5% (w/w), based on the weight of the non-volatile components.

60. The nail varnish of claim 56, wherein said antiviral agent is

61. The nail varnish of claim 56, wherein said antiviral agent is present in an amount of from about 0.08% to about 0.8% (w/w), relative to the total weight of the composition.

62. The nail varnish of claim 56, wherein said antiviral agent is present in an amount of from about 0.8% to about 8% (w/w), based on the weight of the non-volatile components.

63. The nail varnish of claim 56, wherein said antipsoriatic agent is selected from the group consisting of alclometasone, amcinonide, betamethasone, clobetasol, clocortolone, desonide, desoximetasone, diflorasone, fluocinolone, fluocinonide, flurandrenolide, halcinonide, hydrocortisone, mometasone, prednicarbate and triamcinolone, salts thereof, derivatives thereof, and mixtures thereof.

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64. The nail varnish of claim 56, wherein said antipsoriatic agent is present in an amount of from about 0.02% to about 2% (w/w), relative to the total weight of the composition.

65. The nail varnish of claim 56, wherein said antipsoriatic agent is present in an amount of from about 0.1% to about 10% (w/w), based on the weight of the non-volatile components.

66. The nail varnish of claim 47, wherein said humectant is selected from the group consisting of glycerol, sorbitol and mixtures thereof.

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67. The nail varnish of claim 47, wherein said humectant is present in an amount of from about 3% to about 15% (w/w), relative to the total weight of the composition.

68. The nail varnish of claim 47, wherein said humectant is present in an amount of from about 5% to about 35% (w/w), based on the weight of the non-volatile components.

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69. The nail varnish of claim 47, wherein said water is present in an amount of less than about 5% (w/w), relative to the total weight of the composition.

70. The nail varnish of claim 47, wherein said water is present in an amount of from about 0.4% to about 25% (w/w), based on the weight of the non-volatile components.

71. The nail varnish of claim 47, wherein said polymeric film-forming agent is selected from the group consisting of hydrophobic (water insoluble) polymers.

72. The nail varnish of claim 71, wherein said hydrophobic (water insoluble) polymer is selected from the group consisting of hydrophobic cellulose derivatives, hydrophobic methacrylic polymers, cellulose acetate phthalate, shellac, derivatives thereof, and mixtures thereof.

73. The nail varnish of claim 72, wherein said hydrophobic cellulose

derivative is selected from the group consisting of ethyl cellulose of any acceptable molecular weight.

74. The nail varnish of claim 72, wherein said hydrophobic methacrylic polymer is selected from the group consisting of methacrylic acid copolymer type B (USP/NF), methacrylic acid copolymer type C (USP/NF), ammonio methacrylate copolymer type B (USP/NF) and ammonio methacrylate copolymer type A (USP/NF), derivatives thereof, and mixtures thereof.

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A18 } 75. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in an amount of less than about 7.5% (w/w), relative to the total weight of the composition.

76. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in an amount of from about 8% to about 35% (w/w), based on the weight of the non-volatile components.

77. The nail varnish of claim 47, wherein said polymeric

film-forming agent is present in a weight ratio of polymer to antifungal agent from about 1:0.01 to about 1:0.3.

78. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to keratolytic agent from about 1:0.01 to about 1:1.

79. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antibacterial agent from about 1:0.01 to about 1:0.3.

80. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antiviral agent from about 1:0.02 to about 1:0.2.

81. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antipsoriatic agent from about 1:0.006 to about 1:0.15.

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82. The nail varnish of claim 47, wherein said at least one additional excipient is selected from the group consisting of plasticizers.

83. The nail varnish of claim 82, wherein said plasticizer is selected from the group consisting of dibutyl sebacate, diethyl phthalate, lanolin alcohols, mineral oil, petrolatum, polyethylene glycol, propylene glycol, triacetin, triethyl citrate, and mixtures thereof.

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84. The nail varnish of claim 82, wherein said plasticizer is present in an amount of from about 0.1% to about 2% (w/w), relative to the total weight of the composition.

85. The nail varnish of claim 82, wherein said plasticizer is present in an amount of from about 0.5% to about 10% (w/w), based on the weight of the non-volatile components.

86. The nail varnish of claim 82, wherein said plasticizer is present in a weight ratio of plasticizer to polymer from about 0.04:1 to about 0.3:1.

87. The nail varnish of claim 47, wherein said volatile solvent is selected from the group consisting of an alcohol, a ketone, and mixtures thereof.

88. The nail varnish of claim 87, wherein said alcohol is selected from the group consisting of ethanol, isopropyl alcohol, methanol and mixtures thereof, and further wherein said ketone is acetone.

89. The nail varnish of claim 47, wherein said volatile solvent is a mixture of acetone and isopropyl alcohol.

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A20 } 90. The nail varnish of claim 47, wherein said volatile solvent is present in an amount of from about 60% to about 90% (w/w), relative to the total weight of the composition.

91. The nail varnish of claim 89, wherein said acetone and said isopropyl alcohol are present in a volumetric ratio of acetone to isopropyl alcohol from about 1:4 to about 4:1.

92. The nail varnish of claim 47, wherein said solvent system further includes at least one non-volatile solvent selected from the group consisting of benzyl alcohol, benzyl benzoate, corn oil, cottonseed oil, ethyl oleate, glycerin, glycofural, isopropyl myristate, isopropyl palmitate, mineral oil, peanut oil, polyethylene glycol, propylene glycol, propylene carbonate, sesame oil, soybean oil, water, and mixtures thereof.

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A21 > 93. A method of preparing a sustained release varnish or spray formulation for treating the nail and surrounding tissues, comprising the steps of:

- (a) preparing a solution including at least one volatile solvent;
- (b) adding water to the solution prepared in (a);
- (c) dissolving the pharmaceutically effective agents, and excipients in the solution prepared in (b);
- (d) adding the humectant to the solution prepared in (c) when the formulation ingredients are completely dissolved; and
- (e) dissolving the polymeric film forming agents in the solution prepared in (d).

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